Program S-2 Ilmu Kefarmasian
Universitas Pancasila

Farmakokinetik Klinik (2 sks)

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Pustaka

1. Clark B. & Smith A.D. 1986. **An Introduction to Pharmacokinetics**. London; Blackwell Scientific Publications
2. Ritschel W.A. 1986 **Handbook of Basis Pharmacokinetics**. Ed ke-3.Hamilton; Drug Intelligence Publication Inc.
3. Sunil S.J, Philip B.J. 2009. Basic Pharmacokinetics. Pharmaceutical Press
4. Leon Shargel & Andrew B.C.YU. 1988. **Biofarmasetika dan Farmakokinetika Terapan**. Ed ke-2. Fasich & siti Syamsiah, penerjemah. Surabaya: Penerbit Universitas Airlangga. Terjemahan dari: Applied Biopharmaceutics and Pharmacokinetics
5. Hakim L. 2012. **Farmakokinetika Klinik**. Bursa Ilmu Yogyakarta
6. Sulistia G (Editor). 2007. **Farmakologi dan Terapi**. Edisi V. Departemen Farmakologi dan Terapeutik Fakultas Kedokteran Universitas Indonesia.

Bahasan

1. Farmakokinetik
2. Kinetika orde reaksi dan bentuk kurva
3. Parameter farmakokinetik –kertas grafik SL
4. Model Kompartemen
5. Model satu & dua kompartemen terbuka – iv
6. Model satu & dua kompartemen terbuka – ev
7. Ujian Tengah Semester; Closed book

DEFINISI

FARMAKOKINETIKA

- Studi tentang absorbsi, distribusi, metabolisme dan ekskresi
- Ilmu yang mempelajari tentang kinetika absorpsi, distribusi, metabolisme dan ekskresi obat.
- Aplikasi matematik dan pemodelan data kadar obat yang terukur di dalam studi absorpsi, distribusi, metabolisme dan ekskresi obat.

FARMAKODINAMIKA

- Hubungan antara konsentrasi obat dan respon farmakologi
- Ilmu yang mempelajari tentang pengaruh/efek obat terhadap tubuh untuk menghasilkan respon farmakologi

FARKMAKOKINETIKA KLINIK

Ilmu yang mempelajari tentang aplikasi konsep dan prinsip farmakokinetika pada manusia untuk mendisain regimen dosis secara idividual dengan respon terapi yang optimum dari suatu pengobatan dengan reaksi obat merugikan yang minimal

TUJUAN FARMAKOKINETIK
(Basic Science)

- Mempelajari waktu perjalanan obat, kadar obat, kadar metabolit dan jumlahnya di dalam cairan biologik, jaringan dan sekret, serta respon farmakologi.

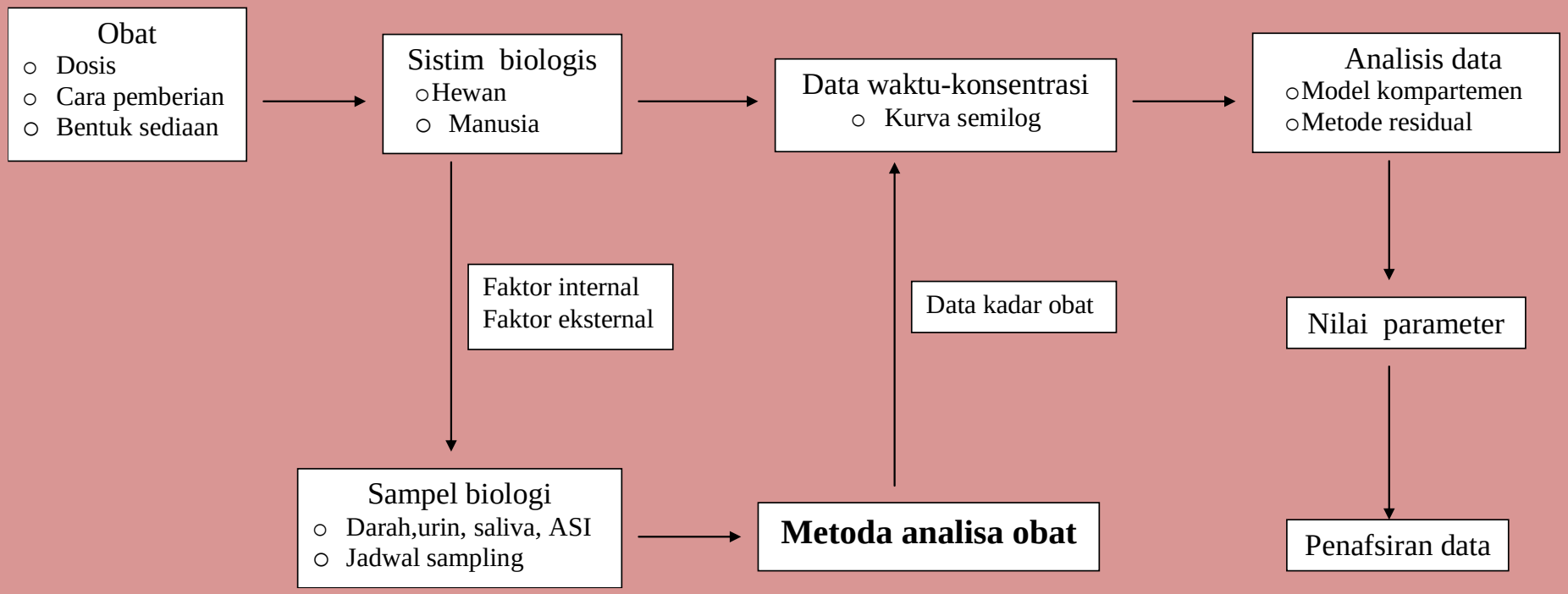
- Menentukan model farmakokinetika obat yang sesuai untuk menginterpretasikan data dari kadar obat yang terukur.

Aplication of pharmacokinetics studies include:

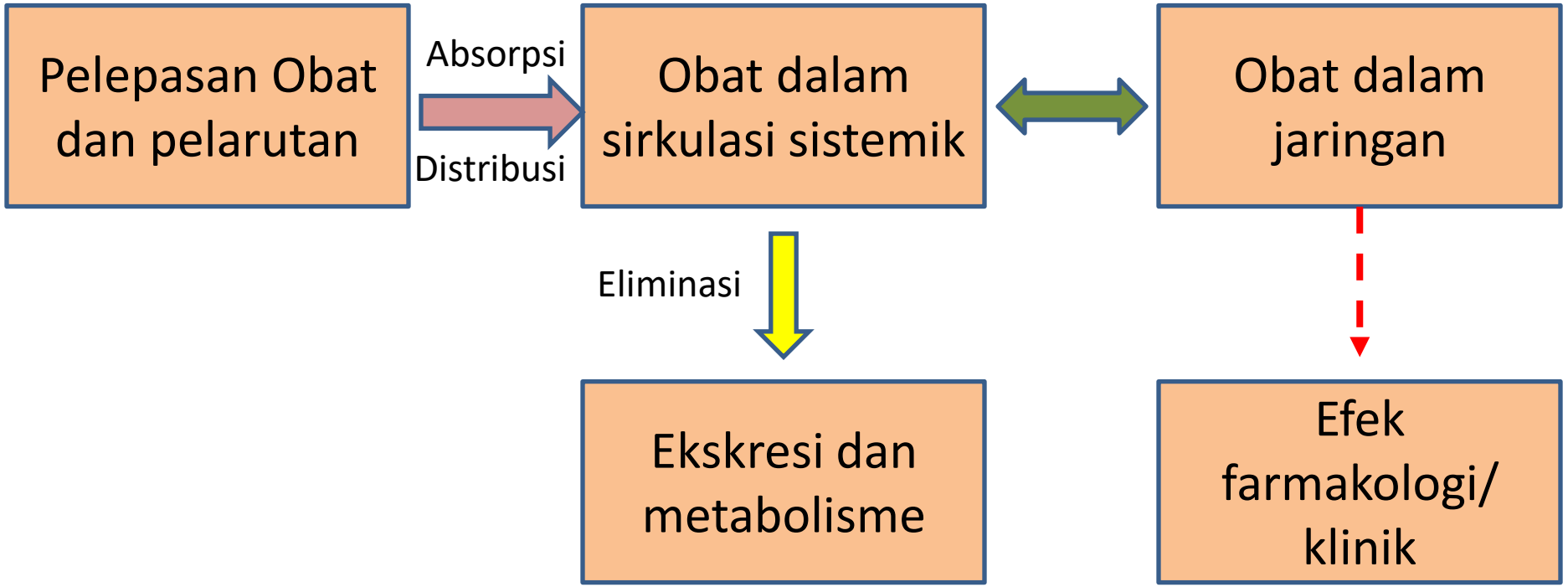
- Bioavalability measurements;
- Effects of physiological and pathological conditions on drug disposition and absorption;
- Dosage adjustment of drugs in disease state, if and when necessary;
- Correlation of pharmacological responses with administration doses;
- Evaluation of drug interaction;
- Clinical prediction using pharmacokinetics parameters to individualize the drug dosing regimen and thus provide the most effective drug therapy

Analisis Farmakokinetik

PKOD/TDM- Standar Pelayanan Kefarmasian di – RS (PMK 72-2016)



Hubungan bentuk sedian obat → efek farmakologi /Terapi



LIBERATION A D M E RESPON

Farmasetika-Biofarmasetika–Farmakokinetika -------Farmakodinami

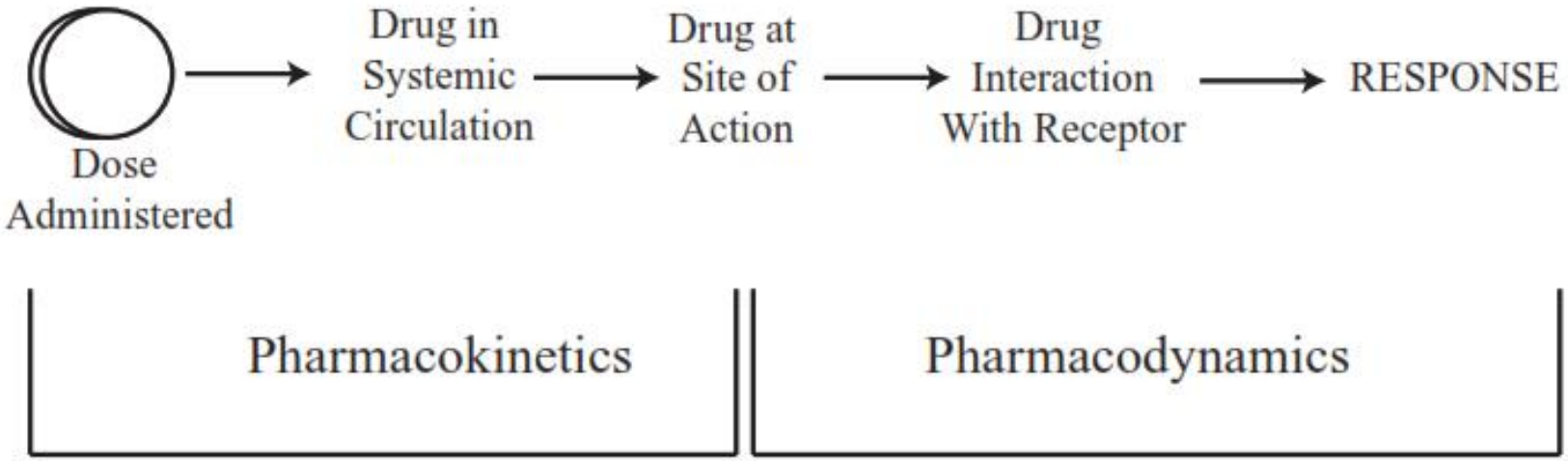
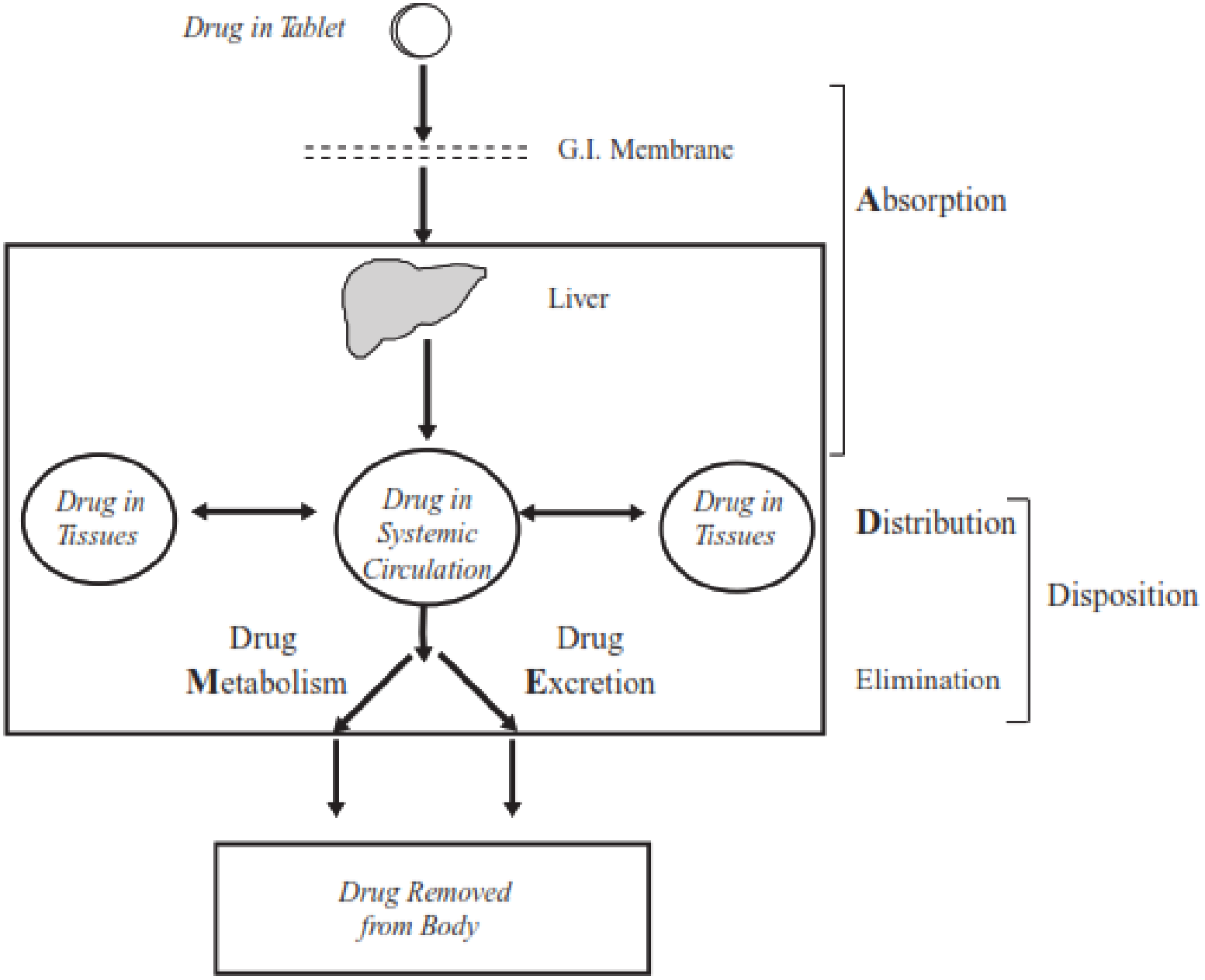


FIGURE 1.1 The two phases of drug action. The pharmacokinetic phase is concerned with the relationship between the value of the dose administered and the value of the drug concentrations achieved in the body; the pharmacodynamic phase is concerned with the relationship between drug concentrations at the site of action and the onset, intensity, and duration of drug response.

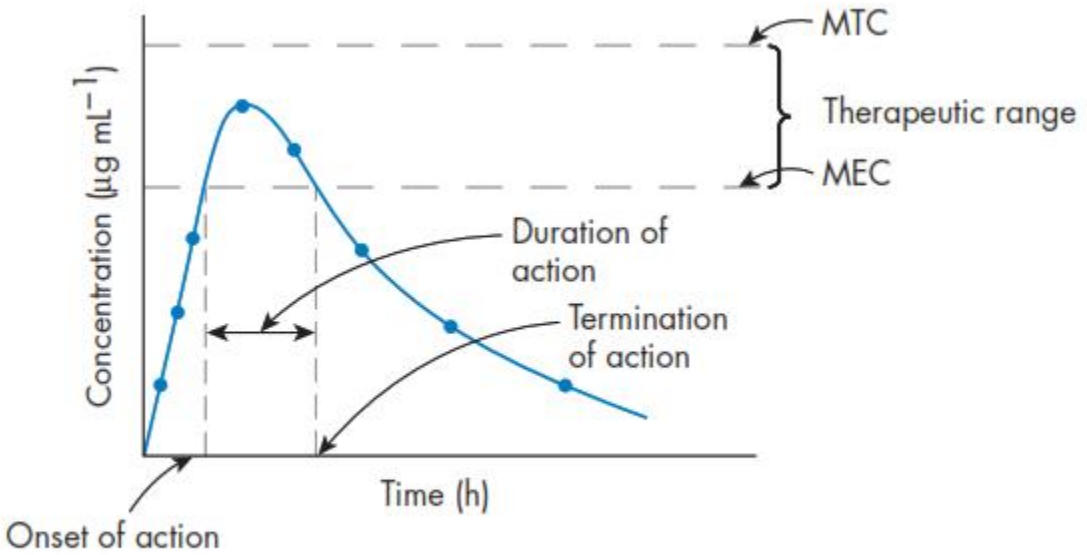

Drug in Tablet
G.I. Membrane
Absorption
Liver
Drug in Tissues
Drug in Systemic Circulation
Drug in Tissues
Distribution
Disposition
Drug Metabolism
Drug Excretion
Elimination
Drug Removed from Body

Konstata=K (Rate/tetapan)

Table 1.3 Values for parameters over time in zero- and first-order processes

Time (h)	Zero order		First order	
	X (mg)	dX/dt (mg h^{-1})	X (mg)	dX/dt (mg h^{-1})
0	100	–	100	–
1	90	10	90	10
2	80	10	81	9
3	70	10	72.9	8.10
4	60	10	65.61	7.29
5	50	10	59.05	6.56
6	40	10	53.14	5.91
7	30	10	47.82	5.32
8	20	10	43.04	4.78
9	10	10	38.74	4.30

Gambar data table 1.3 masing-masing pada kertas grafik rectangular dan kertas grafik semilog (SL). Cari presamaan garis regresi dan nilai t½ (waktu paruh)!



Indeks Terapi (IT)

Figure 1.1 A typical plot (rectilinear paper) of plasma concentration versus time following the administration of a drug by an extravascular route. MTC, minimum toxic concentration; MEC, minimum effective concentration.

Table 1.1 The therapeutic range of selected drugs

Drug	Therapeutic use	Therapeutic range
Tobramycin (Nebcin, Tobrex)	Bactericidal–antibiotic	4–8 mg L^{-1}
Digoxin (Lanoxin)	Congestive heart failure (CHF)	1–2 µg L^{-1}
Carbamazepine (Tegretol)	Anticonvulsant	4–12 mg L^{-1}
Theophylline	Bronchial asthma	10–20 mg L^{-1}

Sumber: Sunil S & Philip J. 2009. Basic Pharmacokinetics . PP. p. 3

Kinetika order nol (Zero order)

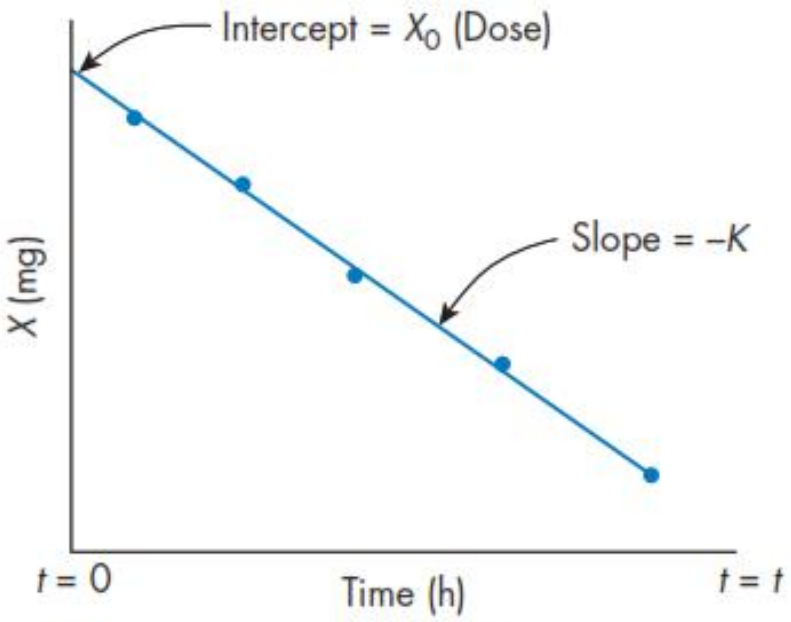


Figure 1.15 Rectilinear graph (R.L.) of zero-order process. *X*, concentration of drug; *K*, rate constant.

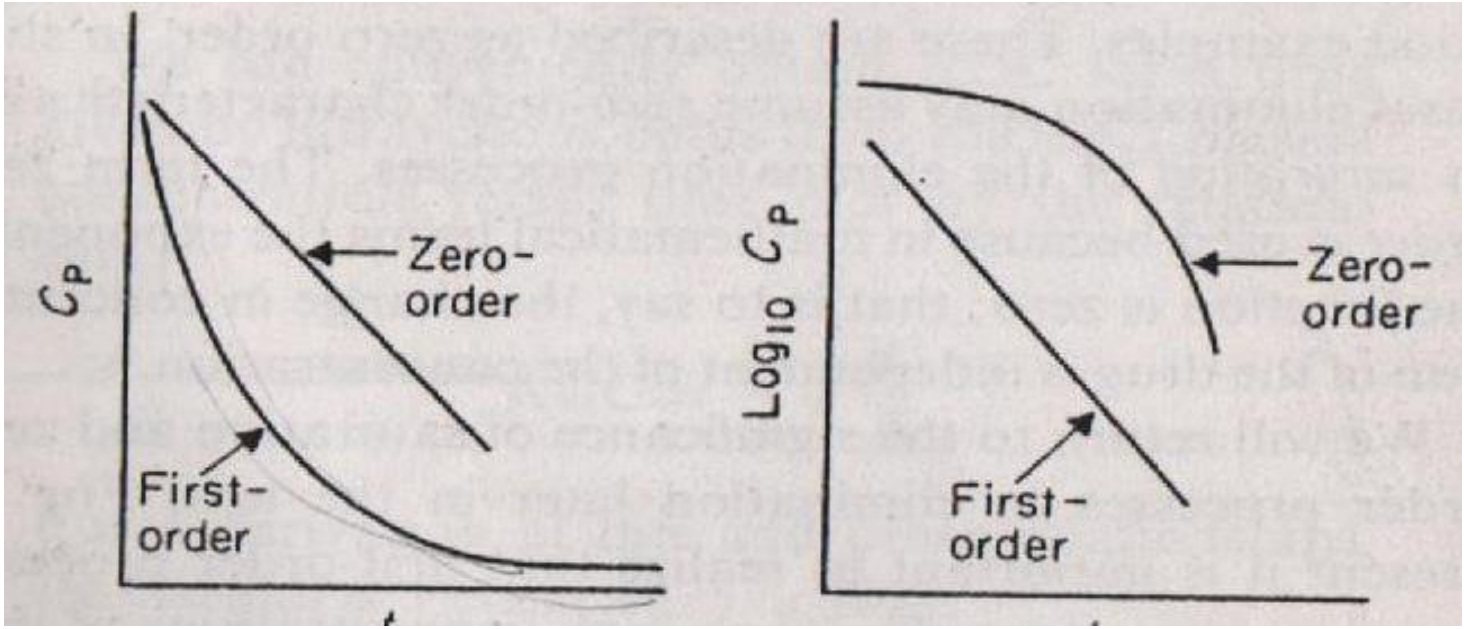
$$X \xrightarrow{K_0} \text{Product (b)}$$

where *X* is a substance undergoing a change

$$X \xrightarrow{K_0} X \text{ (in another location)}$$

where *X* is a substance undergoing transfer

Fiaure 1.14 Process of chanae (zero order).



Kurva zero dan first order pada kertas grafik koordinat rectangular (kiri) dan koordinat semilog (kanan)

Table 1.2 Comparison of zero-order and first-order reactions

Terms	Zero order	First order
$-dX/dt$	$=K_0$ (Eq. 1.10); rate remains constant	$=KX$ (Eq. 1.17); rate changes over time
rate constant	$=K_0$ (unit $=$ mg h^{-1})	$=K$ (unit $=h^{-1}$)
X	$X=X_0-Kt$ (Eq. 1.11) (integrated equation)	$\ln X=\ln X_0-Kt$ (Eq. 1.19) or $\log X=\log X_0-Kt/2.303$ (Eq. 1.20) (integrated equation)
X_0	Assume is 100 mg or 100%	Assume is 100 mg or 100%
rate	K_0=10 mg h^{-1}	K=0.1 h^{-1} or 10% of the remaining X

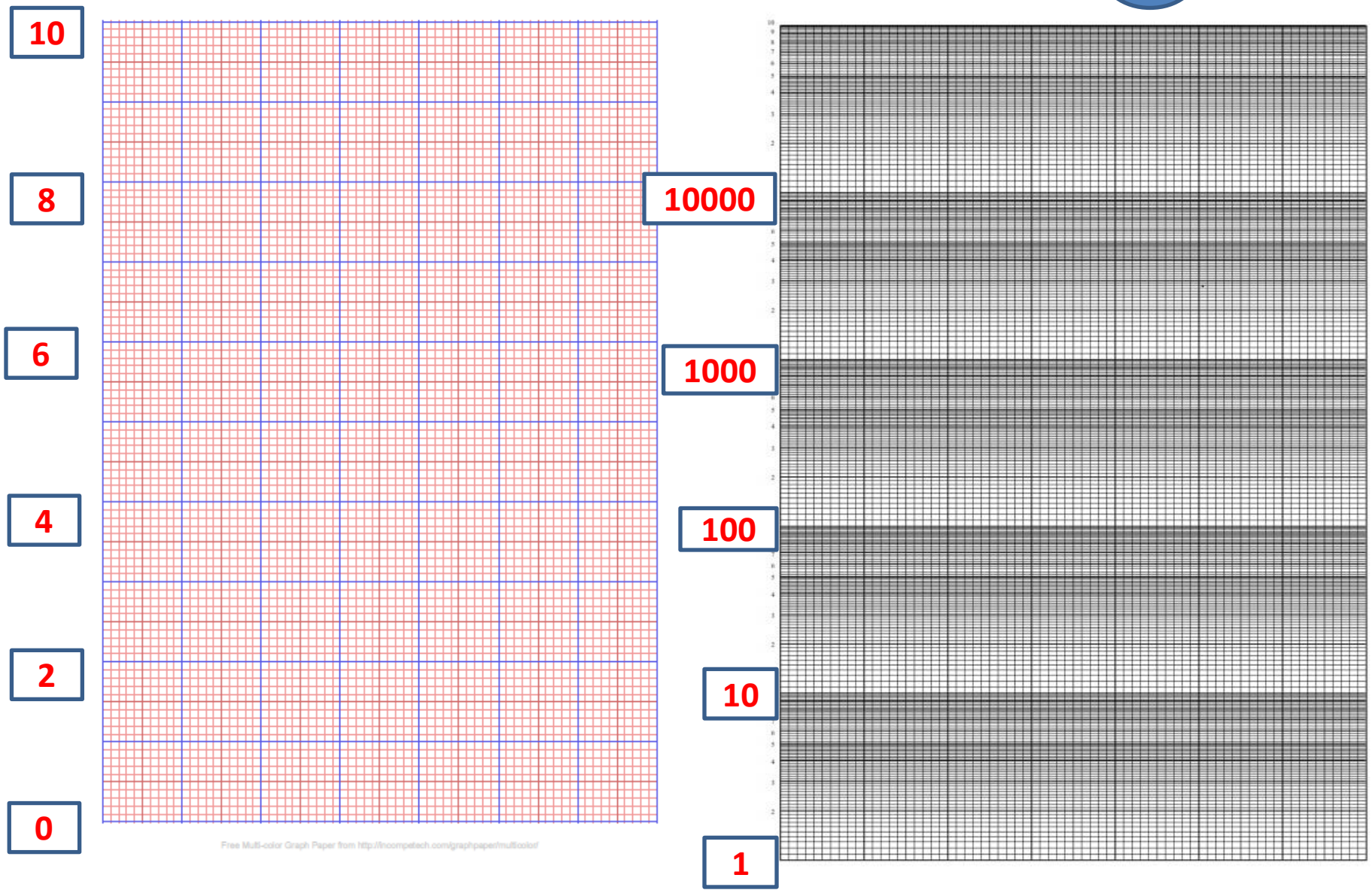
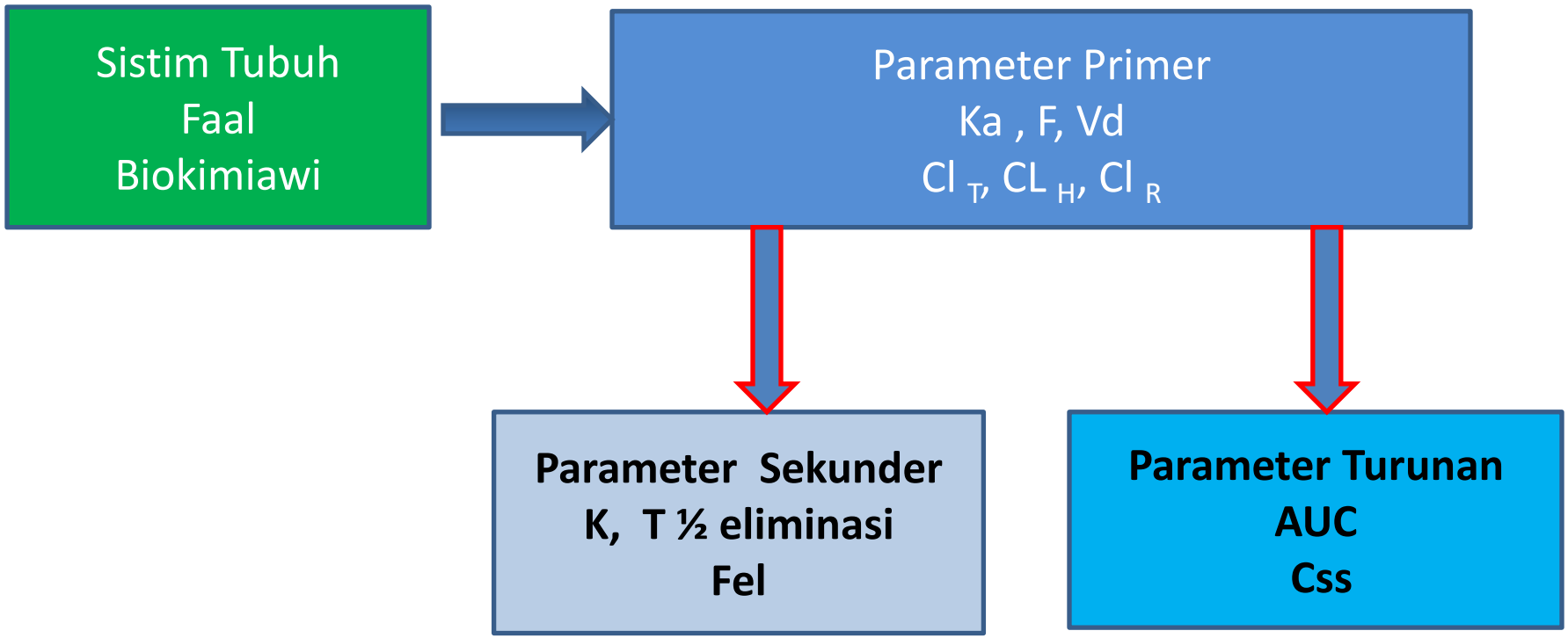

10
8
6
4
2
0
10000
1000
100
10
1
Free Multi-color Graph Paper from http://incompetech.com/graphpaper/multicolor/

Table 2.3 Exponents and logarithms

Rule	Example
$n^a \cdot n^b = n^{a+b}$	$10^1 \cdot 10^2 = 10^3$
$\frac{n^a}{n^b} = n^{a-b}$	$\frac{10^4}{10^2} = 10^2$
$(n^a)^b = n^{ab}$	$(10^3)^2 = 10^6$
$\frac{1}{n^a} = n^{-a}$	$\frac{1}{10^2} = 10^{-2}$
$\sqrt[a]{n} = n^{1/a}$	$\sqrt{n} = n^{1/2}$; $\sqrt{100} = 100^{1/2} = 10$ $\sqrt[3]{n} = n^{1/3}$; $\sqrt[3]{1000} = 1000^{1/3} = 10$
$\log ab = \log a + \log b$	$\log 1000 = \log 10 + \log 100 = 3$
$\log\left(\frac{a}{b}\right) = \log a - \log b$	$\log 10 = \log 1000 - \log 100 = 1$
$\log (a^b) = b(\log a)$	$\log (10^2) = 2(\log 10) = 2$
$-\log\left(\frac{a}{b}\right) = +\log\left(\frac{b}{a}\right)$	$-\log\left(\frac{10}{1000}\right) = \log\left(\frac{1000}{10}\right) = 2$
$\log (10^a) = a$	$\log (10^3) = 3$
$\ln(e^a) = a$	$\ln(e^3) = 3$
$\log a = \frac{\ln a}{2.303}$	$\log 10 = \frac{\ln 10}{2.303} = 1$
$n^0 = 1$	$10^0 = e^0 = 1$
$\ln(n \leq 0) = undefined$	
$\log(n \leq 0) = undefined$	

Parameter Farmakokinetik
Besaran yang diturunkan secara matematis dari hasil pengukuran kadar obat dalam darah



Sumber LH; Hal. 163 (Rowland & Tozer,1995)

Tabel 3.12. Ketergantungan parameter primer terhadap faktor hayati (Rowland & Tozer,1995)

Parameter primer	Faktor hayati (faal dan biokimiawi)
ka	Aliran darah di tempat absorpsi , kecepatan pengosongan lambung dan motilitas usus
F	Kecepatan pengosongan lambung, sekresi asam lambung, enzim hidrolisis, motilitas usus
Vd	Ikatan obat oleh protein plasma dan jaringan, partisi ke dalam lemak, komposisi dan ukuran tubuh
Cl_H	Aliran darah hepatik, ikatan obat oleh darah, aktivitas intrinsik hepatik (metabolisme)
Cl_R	Aliran darah renal, ikatan obat oleh darah, sekresi aktif dan reabsorpsi tubuler, aliran urin dan kecepatan filtrasi glomerulus

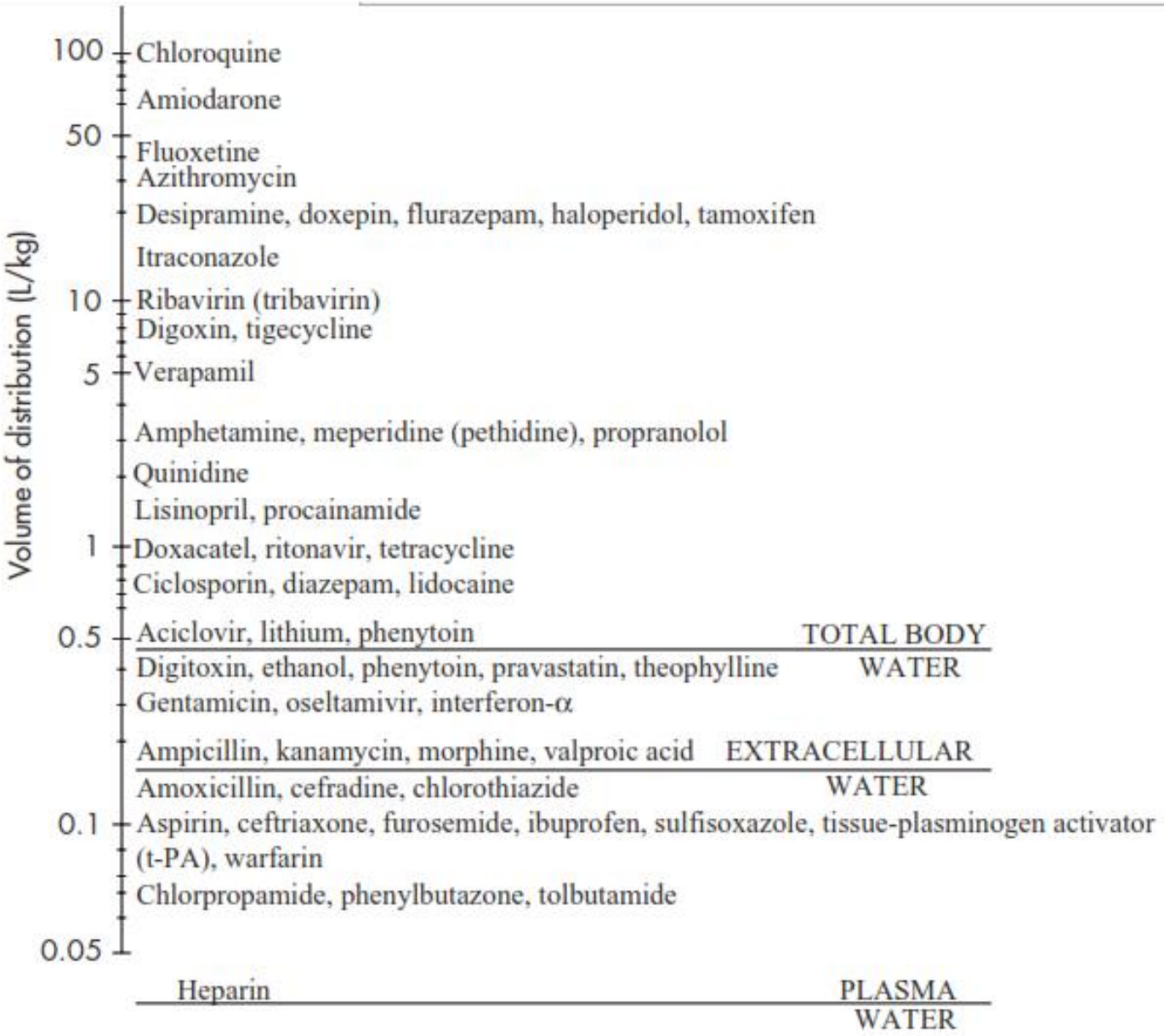


Figure 3.9 The apparent volume of distribution for selected drugs.

Tabel 3.13. Ketergantungan parameter sekunder dan turunan oleh parameter primer (Rowland & Tozer,1995)

Parameter	Persamaan
Sekunder	
K el	Cl/Vd
T ½ eliminasi	0,693.Vd/CL 0,693/Kel
Fel	CL r/CL
Turunan	
AUC	F. Dosis/CL
Css	F. Dosis/λ (interval)

Tugas Latihan Soal 1 kompartemen (IV)

Hakim L. 2012. **Farmakokinetika Klinik**. Bursa Ilmu Yogyakarta

- Latihan hal. 72-74
- Tugas , halaman 75-77 (6 soal)